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Histopathological Characteristics of Japanese Encephalitis in Manchuria in 1945 (Report II)

Grashchenkov, N. I.

In the first article we covered the clinical characteristics of the Manchurian Japanese Encephalitis. In this article we will try to note some of the variations of the central nervous system, noted by us during the Manchurian outbreak in 1945 in 5 sections.

We will not review the clinics of J. encephalitis here.

There are many works on the morphological variations of the central nervous system (Mori, Kawamura, etc).

In the USSR there is one publication on the histopathological variations during Japanese encephalitis in the Far Eastern Primorsk (I. A. Robinson).

Sectioning disclosed hyperemia of the soft brain membranes and brain substance. In particular, the subcortical nodes. In the putamen there were many brownish points, evidently necrosis. In the front lobes there was a brownish tint of the gray substance and hyperemia of the capillaries. A similar tint was noted in the region of the Sylvius aqueduct. The soft membranes were always areas of edema and full of blood. The vessels in the brain, subbrain and spinal region were expanded, held stases. Local hemorrhaging was of a diapedetic character. There were noted perivascular accumulations of erythrocytes without destructive appearances. The walls of the vessels were edematized, with inflamed endothelia; no ruptures in the ~~membranes in the~~ vessels were visible. In two cases there was hemorrhaging in the membranes in the occipital region, rupture of the marginal barrier and penetration of the blood into the soft brain membranes and substance.

The soft brain membranes are infiltrated with microphages, lymphocytes and sometimes by polymorphonuclear leukocytes. The infiltrate penetrates along the vessels from the membranes into the brain substance, thus disrupting the gliomesodermal barrier. In the cortex there is edema of the brain substance. There is injection of the vessels of all calibers, even to the smallest sub-veins. Around the vessels there is an accumulation of liquid exudate, and in places there are granular rosy masses, which, evidently, indicate the disruption of the penetrability. Many stases and hemorrhages are encountered. Often red corpuscle and plasma mixtures are noted with the perivascular infiltrates. There is a great proliferation of the endothelia of the precapillary type vessels.

In the walls of the vessels there are lymphocytes and polyblasts, significant in all cases. In some cases the cells of the infiltrate occupy all the layers of the vessel walls and form branches. In a majority of the cases the inflammatory infiltrates are limited to the intra-adventitial expanse, but, along with this, there are deep disruptions of the barrier functions, when the elements of infiltrate penetrate into the tissue surrounding the brain. This can be seen in the cortex, particularly in the subcortical nodes, in the hypothalamic region and also in the Sommering black substance, and sometimes in the pons varolii and Medulla oblongata.

In the marginal layer there is acute proliferation of the microglia. There is an abundance of bacilli form in the Hortega cells. The nuclei of these cells are often pyknotic and shriveled, appendices are swelled, small clots can be detected.

Along with the diffused proliferation of the Hortega glia and the oligodendroglia, there are significant coagulations with formations of

desintegrations, mainly around the perishing nerve cells. These coagulations form around single cells or around groups of them. There are significant variations of the cells, the plasma is pale and drawn, the nucleus is dark. In the center of the Broca, in the occipital lobes and other sections there are diffused cellular variations, but the greatest is in the frontal lobes.

In all parts of the brain there are areas of softening. In these regions, particularly in the frontal lobes, the cells are distributed very densely; the majority of them are granular spheres. Often it is possible to note the conversion of Hortega cells into granular spheres. On preparations, tinted according to Shpilmeier, centers of necrosis are connected with the vessels; due, evidently, to the disruption of the blood circulation. Certain types of thromboses of the small vessels confirm this.

In the white subcortex substance there are diffused micro- and macroglial proliferations on the border of the cortex and in deeper sections; in the gray matter it is expressed more so. Here the proliferation affects the oligodendroglia, and also the Hortega cells; the cells of oligodendroglia in the white matter run chain like along the small type vessels, sometimes forming rosettes. In the internal capsule there is infiltration of the walls of the veins. Around such vessels there is sometimes a glial wall, consisting of Hortega cells. The oligodendroglia are edematized (surrounded by cells with perinuclear lucid intervals).

In the cortex and white subcortex matter there are variations of the astrocytes; they lose their appendices, curve, take a spherical form. If the appendices remain, they will swell at the end and often vary.

The Subcortical Nodes—Putamen and Pineal Body. Perivascular infiltration acutely expressed; infiltration consists of lymphocytes mainly.

There is separation of the endothelial cells. In some cases it is possible to note fibrinoid swelling of the vessel walls. Diffused proliferation of the Hortega cells and oligodendroglia is acute. Great quantities of these small nodules of these elements are located around the capillaries. Sometimes this tie is not completed, then the nodules have a porous build. The Hortega cells are swelled, often in the form of rods, with small quantities of side branches with dull ends. The nuclei of the cells have a long form, untrue, often bean shaped. Often there is pyknosis of the nuclei, as if they were fragmentated. They have a segmentated appearance, they have a half-moon shape, appear like polymorphonuclear leukocytes. The cells are either lacking plasma or the latter has a surrounding form. Sometimes the Hortega cells with the pyknotic nuclei are quantitatively formed into nodes (small clumps). The oligodendroglia cells, encountered in smaller numbers in these ganglion, are swelled, sometimes with shortened appendices. In some ganglion the Hortega cells, the body of which is curved and the appendices shortened, posses appendices only on one side. Some of these cells have been seen without appendices and curved. These cells have a latticed structure of plasma and a decreased dark nucleus, sometimes of an untrue, shrivelled form, bean shaped or half-moon. These cells are of the latticed type. The change of the Hortega cells, consisting of granulomas, into latticed cells and granular spheres is visible. During tinting with scarlet, granular clots are found in the plasma of the latter. In places there are centers of softening in which there are single varied Hortega cells.

In one case the gliosis nodes and the areas of softening were only lightly expressed. Here, as in the cortex, the proliferation of the Hortega glia is expressed greater, representing degeneration with

pyknotic nuclei. In the putamen there is a great quantity of small centers of necrosis with karyorrhexis of the nuclei. In these centers there are capillary type vessels with pyknosis of the endothelia. In the periphery of some of the necrotic centers there are accumulations of Hortega cells. The nerve cells in the area surrounding these centers are diffusely varied; the cells discharge in places. The cells in the area of the inflamed ganglions suffer badly, in the putamen, the big as well as the little cells are involved. The oligodendroglia and Hortega glia surround the ganglionic cells, forming neuronophagic nodes.

Pallidum. Neuronophagic nodes represented in small numbers. The nerve cells are slightly varied in comparison with the putamen. There is non-specific variation of the cells (hyperchromatosis of nuclei, chromatolysis), but, the diffused proliferation of the oligodendroglia and Hortega cells is present. Areas of softening are smaller. Edema of some type in some cells.

Thalamus. Variations more severe than in Pallidum. Vessels full of blood and contain stases. Walls of vessels edematized, some places there are hyaline thrombi. Hemorrhagings, sometimes around the infiltrated vessels. Infiltrates consist mainly of lymphoid elements, surrounded by accumulations of Hortega cells and oligodendroglia. Some hypertrophic astrocytes noted; sometimes they are proliferated.

The ganglionic cells suffer mostly near the inflammatory centers. Along with the clear neuronophages there are certain cells surrounded by glial elements. There is a diffused variation of the nerve cells. There is great proliferation of the oligodendroglia and Hortega cells. Expansive centers of softening with the formation of granular spheres.

Hypothalamic Region. The proliferative component is strongly present. It is detected in the proliferation of the elements of the vessel

walls, which are participating in the formation of expressed infiltrates, distributed in the adventitial expanse. Sometimes the vessel walls are continuously infiltrated. Around such vessels there is a great proliferation of Hortega cells with very strong hypertrophic appendices. There are neuronophagic nodes. In the nucleus tuber tuberculi in the mamillary bodies there are degenerative variations of part of the nerve cells. Many cells have dark nuclei and pale, poorly tinted plasma. On the very bottom of the III ventricle under the nuclei there are gliosis reactions noted in all cases. In 2 cases the proliferative variations in the hypothalamic region were replaced by degenerative variations which were well represented.

Black Sommering Substance. There is swelling and proliferation of the cells of the endothelia, places there are hemorrhages from the vessels with infiltrated walls. Variations of the cells of the black substance are severe. Here there is a discharge of the cells, particularly of the medial portion, where there is a continuous discharge, and in singular remaining cells there are dark nuclei, discharge of pigment, individual appendices or curved remains of cells. In these sections there is a high, diffused outgrowth of Hortega glia, while in the perivascular centers there are no accumulations. These Hortega cells are sometimes hypertrophied, but more often degeneratively varied, with dark, fragmented-like nuclei. There are great quantities of granular spheres or accumulations of granular spheres. Near these spheres there are accumulations, the centers of which are noted to have clots of pigment, distributed freely, sometimes incorporated in the granular sphere. There are neuronophagic nodes, consisting of oligodendroglia cells and Hortega glia. In some places the black substance tissues are softened. In areas of less affection the proliferation of the Hortega glia is diffused, degenerative variations, depigmentation, neuronophagic nodes, discharge

of cells. In some cases there was an asymmetry of affection between the right and left sides.

On preparations, tinted according to Shpilmeier, the swelling of the myelinic fibers is noted, these are located in the centers of diffused infiltration, which exceeds the limits of the vessel walls. The nuclei of the III and IV pairs of cranial nerves are varied slightly. Some cells are shriveled, there is hyperchromatosis of the nucleus.

Red Nucleus. A great part of the cells are secure. There are individual nodes, consisting of Hortega cells with conversions to granular spheres. Great diffused proliferation of glia and microglia. The process is basically less than in the black substance.

Corpora Quadrigemina. Singular variations of cells. Proliferation of glia and macroglia is diffused and in centers with formations of nodes. Converting into granular spheres. In the white substance a small infiltration of lymphocytes around the vessels. Cells of the ependymal layers are pyknotic, lightly proliferated.

Pons. The cells of the nucleus of the facial nerve remained secure. Among them there are single glious nodes. The basic mass of the reticular substance remained unchanged. Great centers of diffused proliferation of Hortega cells with degeneration of them were noted in the nucleus of the brain. In the region of the pyramidal tracts there were stases in the vessels.

On preparations, tinted according to Shpilmeier, there were visible small centers of demyelination. There was some increase of the marginal cells, adjacent to the infiltrated soft brain membranes.

Medulla Oblongata. Great proliferation of glia, mainly Hortega cells. There are mixed nodes, consisting of Hortega cells and oligodendroglia.

Cells of the nuclei of the IX, X and XII pairs are varied slightly, but there is a cell discharge. Many neuronophagic nodes. Great proliferation of astrocytes and microglia. In the olives there is a great variation of the nerve cells. Almost everywhere there is pyknosis of the nuclei; Nissle's degeneration. Great proliferation of glia, mainly oligodendroglia. There are nodes in the coils of the olives, consisting of Hortega and oligodendroglia. The vestibular nuclei are varied slightly. Throughout the medulla oblongata there is edema and ruptured tissue. On the bottom of the IV ventricle there is some subependymal gliosis.

The variations of the Pons and Medulla noted here were prevalent in three cases, 2 cases had more severe variations.

Cerebellum. Expressed meningitis among the fissures. The infiltrate consists of macrophages, lymphocytes and some plasmatic cells. In the white substance there is proliferation by astrocytic glia and oligodendroglia. In places there are nodes of Hortega cells. In the zone of the Purkinje there is an expansive discharge of cells and their variation; in places the ganglionic cells are absent, places their nuclei are very pyknotic, the nuclear capsule is indistinguishable, the chromatin is in the plasma. There is a significant proliferation of the cells of the oligodendroglia.

In the cells of the dentate nucleus there are nodes consisting of oligodendroglia and Hortega elements. Significant diffused proliferation of these cells, pyknosis of the nuclei. In the ganglionic cells-- a field of discharge.

Spinal Cord. Proliferation of the cellular elements in the roots of the neck section of the spinal cord, and also in the shoulder area.

There are small hemorrhages. In the soft brain membranes there is an expressed meningitis. In the area of the forward horns—diffused proliferation; on the edge of the proliferation there is neuronophagia; the neuronophagic nodes are frequent in the front horns, while in the rear and side there are less. The inflammatory process is more visible in the neck and shoulder area. Many ganglionic cells are varied; they are in the stage of severe infection, according to Nissle. In contrast to Tsak encephalitis, a majority of the cells are untouched. The perivascular infiltration of the vessel walls in the white and gray matter is also observed in those membranes around the smaller veins. The infiltrates are mainly plasma lymphoid elements; in some cases there is participation of the plasmatic cells. The latter enter into the tissue of the brain substance. Hyperplasia of the adventitial cells can be noted, their nuclei are pyknotic and swelled.

Resume. Thus, the process is characterized, other than by the appearances of proliferation, by the severe circulatory disruptions, particularly by the tendency for the destructive variations of the histocytes of the brain and the Hortega cells, as well as the nerve cells. The region most severely affected is the central brain, particularly the Sommering Black substance, putamen, thalamus, hypothalamus region and, in some cases, the pons and medulla. The process is evident in the cortex also, and in the subcortex. The above syndrome, constituted by microscopy, explains the clinical symptoms which are observed during the severe course of infection.

Comparatively similar histopathological and virusological aspects were noted during analysis of the Original J. encephalitis and that in Manchuria. Even the virus was identical.

However, our described histopathological and clinical aspects do differ from those of Ekonomo encephalitis. Therefore, these two different infections should not be confused.

No tables, footnotes, etc.; complete translation.